Applicant: Leake et al.

Serial No.: 10/613,077

Filing Date: 01 July 2003

**Supplemental Preliminary Amendment** 

February 20, 2004

Page 2 of 9

**Amendments to the Specification:** 

On page 1, replace the paragraph spanning lines 6-7 with the following amended

paragraph:

This application <del>claims priority to</del> is a continuation-in-part of U.S. Patent

Application Seral No. 10.406,908, filed 02 April 2003, which is hereby incorporated by

reference.

On page 6, replace the paragraph spanning lines 22-26 with the following amended

paragraph:

In yet another embodiment, the invention provides [[A]] a method of performing

RNA interference, said mathod comprising exposing a double stranded polynucleotide to

a target nucleic acid, wherein said double stranded polynucleotide is comprised of a sense

strand and an antisense strand, and wherein said sense strand is substantially

nonfunctional.

On page 41, replace the paragraph spanning lines 21-22 with the following amended

paragraph:

The sense strand can further comprise[[s]] a cap on its 3' end. Preferably, the cap

is an inverted deoxythymidine (idT) or two consecutive 2'-O-methyl modified bases at

the end positions (nucleotides 18 and 19).[[.]]

Applicant: Leake et al. Serial No.: 10/613,077 Filing Date: 01 July 2003

Supplemental Preliminary Amendment February 20, 2004

Page 3 of 9

Please replace Table 4, beginning on page 61, with the following amended Table

4:

Table 4: Constructs for 2'-Deoxy Modifications/fLUC		
Identifier	Sequence	SEQ. ID NO.
fLUC5-AS 3D19	uuuaugaggaucucucdudgdadtdt	27
fLUC5-AS 3D16	uuuaugaggaucucudcdudgadtdt	28
fLUC5-AS 3D13	uuuaugaggaucdudcducugadtdt	29
fLUC5-AS 3D10	uuuaugaggdadudcucucugadtdt	30
fLUC5-AS 3D7	uuuaugdadgdgaucucucugadtdt	31
fLUC5-AS 3D4	uuudadudgaggaucucucugadtdt	32
fLUC5-AS 3D1	dududuaugaggaucucucugadtdt	33
fLUC5-AS 2D19	uuuaugaggaucucucudgdadtdt	34
fLUC5-AS 2D17	uuuaugaggaucucucdudgadtdt	35
fLUC5-AS 2D15	uuuaugaggaucucdudcugadtdt	36
fLUC5-AS 2D13	uuuaugaggaucdudcucugadtdt	37
fLUC5-AS 2D11	uuuaugaggadudcucucugadtdt .	38
fLUC5-AS 2D9	uuuaugagdgdaucucucugadtdt	39
fLUC5-AS 2D7	uuuaugdadggaucucucugadtdt	40
fLUC5-AS 2D5	uuuadudgaggaucucucugadtdt	41
fLUC5-AS 2D3	uududaugaggaucucucugadtdt	42
fLUC5-AS 2D1	duduuaugaggaucucucugadtdt	43
fLUC5-AS 1D19	uuuaugaggaucucucugdadtdt	44
fLUC5-AS 1D18	uuuaugaggaucucucudgadtdt	45
fLUC5-AS 1D17	uuuaugaggaucucucdugadtdt	46
fLUC5-AS 1D16	uuuaugaggaucucudcugadtdt	47
fLUC5-AS 1D15	uuuaugaggaucucducugadtdt[[2]]	48
fLUC5-AS 1D14	uuuaugaggaucudcucugadtdt	[[48]] <u>49</u>

Applicant: Leake et al.
Serial No.: 10/613,077
Filing Date: 01 July 2003
Supplemental Preliminary Amendment
February 20, 2004
Page 4 of 9

fLUC5-AS 1D13	uuuaugaggaucducucugadtdt	50
fLUC5-AS 1D12	uuuaugaggaudcucucugadtdt	51
fLUC5-AS 1D11	uuuaugaggaducucucugadtdt	52
fLUC5-AS 1D10	uuuaugaggdaucucucugadtdt	53
fLUC5-AS 1D9	uuuaugagdgaucucucugadtdt	54
fLUC5-AS 1D8	uuuaugadggaucucucugadtdt	55
fLUC5-AS 1D7	uuuaugdaggaucucucugadtdt	56
fLUC5-AS 1D6	uuuaudgaggaucucucugadtdt .	57
fLUC5-AS 1D5	uuuadugaggaucucucugadtdt	58
fLUC5-AS 1D4	uuudaugaggaucucucugadtdt	59
fLUC5-AS 1D3	uuduaugaggaucucucugadtdt	60
fLUC5-AS 1D2	uduuaugaggaucucucugadtdt	61
fLUC5-AS 1D1	duuuaugaggaucucucugadtdt	62
fLUC5-S 3D19	ucagagagauccucaudadadadtdt	63
fLUC5-S 3D16	ucagagagauccucadudadaadtdt	64
fLUC5-S 3D13	ucagagagauccdudcdauaaadtdt	65
fLUC5-S 3D10	ucagagagadudcdcucauaaadtdt	66
fLUC5-S 3D7	ucagagdadgdauccucauaaadtdt	67
fLUC5-S 3D4	ucadgdadgagauccucauaaadtdt	68
fLUC5-S 3D1	dudcdagagagauccucauaaadtdt	69
fLUC5-S 2D19	ucagagagauccucauadadadtdt	70
fLUC5-S 2D17	ucagagagauccucaudadaadtdt	71
fLUC5-S 2D15	ucagagagauccucdaduaaadtdt	72
fLUC5-S 2D13	ucagagagauccdudcauaaadtdt	73
fLUC5-S 2D11	ucagagagaudcdcucauaaadtdt	74
fLUC5-S 2D9	ucagagagdaduccucauaaadtdt	75
fLUC5-S 2D7	ucagagdadgauccucauaaadtdt	76
fLUC5-S 2D5	ucagdadgagauccucauaaadtdt	77
fLUC5-S 2D3	ucdadgagagauccucauaaadtdt	78

Applicant: Leake et al. Serial No.: 10/613,077
Filing Date: 01 July 2003
Supplemental Preliminary Amendment

February 20, 2004

Page 5 of 9

fLUC5-S 2D1	dudcagagagauccucauaaadtdt	79
fLUC5-S 1D19	ucagagagauccucauaadadtdt	80
fLUC5-S 1D18	ucagagagauccucauadaadtdt	81
fLUC5-S 1D17	ucagagagauccucaudaaadtdt	82
fLUC5-S 1D16	ucagagagauccucaduaaadtdt	83
fLUC5-S 1D15	ucagagagauccucdauaaadtdt	84
fLUC5-S 1D14	ucagagagauccudcauaaadtdt	85
fLUC5-S 1D13	ucagagagauccducauaaadtdt	86
fLUC5-S 1D12	ucagagagaucdcucauaaadtdt	87
fLUC5-S 1D11	ucagagagaudccucauaaadtdt	88
fLUC5-S 1D10	ucagagagaduccucauaaadtdt	89
fLUC5-S 1D9	ucagagagdauccucauaaadtdt	90
fLUC5-S 1D8	ucagagadgauccucauaaadtdt	91
fLUC5-S 1D7	ucagagdagauccucauaaadtdt	92
fLUC5-S 1D6	ucagadgagauccucauaaadtdt	93
fLUC5-S 1D5	ucagdagagauccucauaaadtdt	94
fLUC5-S 1D4	ucadgagagauccucauaaadtdt	95
fLUC5-S 1D3	ucdagagagauccucauaaadtdt	96
fLUC5-S 1D2	udcagagagauccucauaaadtdt	97
fLUC5-S 1D1	ducagagagauccucauaaadtdt	98
A "d" indicates that the nucleotide following the "d" is deoxy at the 2' position.		

Applicant: Leake et al. Serial No.: 10/613,077 Filing Date: 01 July 2003 Supplemental Preliminary Amendment February 20, 2004

Page 6 of 9

Please replace Table 5, beginning on page 64, with the following amended Table 5:

Table 5: Constructs for 2'-O-Methyl Modifications/fLUC		
Identifier	Sequence	SEQ. ID NO.
fLUC5-AS 3M19	uuuaugaggaucucucmumgmadtdt	99
fLUC5-AS 3M16	uuuaugaggaucucumcmumgadtdt	100
fLUC5-AS 3M13	uuuaugaggaucmumcmucugadtdt	101
fLUC5-AS 3M10	uuuaugaggmamumcucucugadtdt	102
fLUC5-AS 3M7	uuuaugmamgmgaucucucugadtdt	103
fLUC5-AS 3M4	uuumamumgaggaucucucugadtdt	104
fLUC5-AS 3M1	mumumuaugaggaucucucugadtdt	105
fLUC5-AS 2M19	uuuaugaggaucucucumgmadtdt	106
fLUC5-AS 2M17	uuuaugaggaucucucmumgadtdt	107
fLUC5-AS 2M15	uuuaugaggaucucmumcugadtdt	108
fLUC5-AS 2M13	uuuaugaggaucmumcucugadtdt	109
fLUC5-AS 2M11	uuuaugaggamumcucucugadtdt	110
fLUC5-AS 2M9	uuuaugagmgmaucucucugadtdt	111
fLUC5-AS 2M7	uuuaugmamggaucucucugadtdt	112
fLUC5-AS 2M5	uuuamumgaggaucucucugadtdt	[[1113]] <u>113</u>
fLUC5-AS 2M3	uumumaugaggaucucucugadtdt	114
fLUC5-AS 2M1	mumuuaugaggaucucucugadtdt	115
fLUC5-AS 1M19	uuuaugaggaucucucugmadtdt	116
fLUC5-AS 1M18	uuuaugaggaucucucumgadtdt	117
fLUC5-AS 1M17	uuuaugaggaucucucmugadtdt	118
fLUC5-AS 1M16	uuuaugaggaucucumcugadtdt	119
fLUC5-AS 1M15	uuuaugaggaucucmucugadtdt	120
fLUC5-AS 1M14	uuuaugaggaucumcucugadtdt	121
fLUC5-AS 1M13	uuuaugaggaucmucucugadtdt	122
fLUC5-AS 1M12	uuuaugaggaumcucucugadtdt	123

Applicant: Leake et al.
Serial No.: 10/613,077
Filing Date: 01 July 2003
Supplemental Preliminary Amendment
February 20, 2004
Page 7 of 9

fLUC5-AS 1M11	uuuaugaggamucucucuqadtdt	124
	•	
fLUC5-AS 1M10	uuuaugaggmaucucucugadtdt	125
fLUC5-AS 1M9	uuuaugagmgaucucucugadtdt	126
fLUC5-AS 1M8	uuuaugamggaucucucugadtdt	127
fLUC5-AS 1M7	uuuaugmaggaucucucugadtdt	128
fLUC5-AS 1M6	uuuaumgaggaucucucugadtdt	129
fLUC5-AS 1M5	uuuamugaggaucucucugadtdt	130
fLUC5-AS 1M4	uuumaugaggaucucucugadtdt	131
fLUC5-AS 1M3	uumuaugaggaucucucugadtdt	132
fLUC5-AS 1M2	umuuaugaggaucucucugadtdt	133
fLUC5-AS 1M1	muuuaugaggaucucucugadtdt	134
fLUC5-S 3M19	ucagagagauccucaumamamadtdt.	135
fLUC5-S 3M16	ucagagagauccucamumamaadtdt	136
fLUC5-S 3M13	ucagagagauccmumcmauaaadtdt	137
fLUC5-S 3M10	ucagagagamumcmcucauaaadtdt	138
fLUC5-S 3M7	ucagagmamgmauccucauaaadtdt	139
fLUC5-S 3M4	ucamgmamgagauccucauaaadtdt	140
fLUC5-S 3M1	mumcmagagagauccucauaaadtdt	141
fLUC5-S 2M19	ucagagagauccucauamamadtdt	142
fLUC5-S 2M17	ucagagagauccucamumaaadtdt	143
fLUC5-S 2M15	ucagagagauccumcmauaaadtdt	144
fLUC5-S 2M13	ucagagagaucmcmucauaaadtdt	145
fLUC5-S 2M11	ucagagagamumccucauaaadtdt	146
fLUC5-S 2M9	ucagagamgmauccucauaaadtdt	147
fLUC5-S 2M7	ucagamgmagauccucauaaadtdt	148
fLUC5-S 2M5	ucagmamgagauccucauaaadtdt	149
fLUC5-s 2M3	ucmamgagagauccucauaaadtdt	150
fLUC5-S 2M1	   mumcagagagauccucauaaadtdt	151
fLUC5-S 1M19	ucagagagauccucaúaamadtdt	152

Applicant: Leake et al. Serial No.: 10/613,077 Filing Date: 01 July 2003

Filing Date: 01 July 2003 Supplemental Preliminary Amendment

February 20, 2004

Page 8 of 9

fLUC5-S 1M18	ucagagagauccucauamaadtdt	153
fLUC5-S 1M17	ucagagagauccucaumaaadtdt	154
fLUC5-S 1M16	ucagagagauccucamuaaadtdt	155
fLUC5-S 1M15	ucagagagauccucmauaaadtdt	156
fLUC5-S 1M14	ucagagagauccumcauaaadtdt	157
fLUC5-S 1M13	ucagagagauccmucauaaadtdt	158
fLUC5-S 1M12	ucagagagaucmcucauaaadtdt	159
fLUC5-S 1M11	ucagagagaumccucauaaadtdt	160
fLUC5-S 1M10	ucagagagamuccucauaaadtdt	161
fLUC5-S 1M9	ucagagagmauccucauaaadtdt	162
fLUC5-S 1M8	ucagagamgauccucauaaadtdt	163
fLUC5-S 1M7	ucagagmagauccucauaaadtdt	164
fLUC5-S 1M6	ucagamgagauccucauaaadtdt	165
fLUC5-S 1M5	ucagmagagauccucauaaadtdt	166
fLUC5-S 1M4	ucamgagagauccucauaaadtdt	167
fLUC5-S 1M3	ucmagagagauccucauaaadtdt	168
fLUC5-S 1M2	umcagagagauccucauaaadtdt	169
fLUC5-S 1M1	mucagagagauccucauaaadtdt	170

The letter "m" indicates that the nucleotide following the "m" is modified with a 2'-O-methyl moiety.